

## **REMARKS**

In view of the following representations, reconsideration and allowance of the above-identified application is respectfully requested.

Claims 1, 9-10, 12-16 and 34-35 are pending in the present application.

On pages 2-8 of the Office Action, the Examiner rejected claims 1, 9-10, 12-16 and 34-35 under 35 U.S.C. § 103(a) as being unpatentable over United States Published Application No. 2004/0224020 (hereinafter “Schoenhard”) in view of United States Patent No. 5,160,742 (hereinafter “Mazer”)

The current pending claims recite a sustained release oral tablet that consists of three essential structural elements: 1) an oxycodone core; 2) a single delayed release coating surrounding the core; and 3) an immediate release oxycodone coating surrounding the delayed release coating. The claimed tablet may also optionally consist of a final aesthetic or cosmetic coating. This final coating is optional and does not affect the *in vivo* or *in vitro* properties of the claimed dosage form. The oxycodone core must employ a high viscosity binder that gels or swells in the presence of water (a hydrogel). Further, the delayed release coating must employ a combination of two pH dependent materials wherein the first pH dependent material dissolves in a pH between 5 and 7 and the second pH dependent material dissolves at a pH greater than 8. Additionally, the delayed release coating employs a substantial portion of specific inert processing aids.

Applicants have discovered that the unique combination of the recited inert processing aids and two different pH dependent coating materials combined with the a high viscosity hydrogel binder in the core, provides a safe and stable, sustained release oxycodone tablet.

Schoenhard discloses multiparticulate dosage forms containing controlled release granules or beads of oxycodone. The controlled release granules or beads may be further surrounded by a gelatin coating which can contain an immediate release portion of oxycodone. Schoenhard also discloses a laundry list of additional excipients that may be used in combination with the multiparticulate oxycodone dosage forms.

Schoenhard does not specifically disclose high viscosity hydrogel binders in the cores as recited in the claims of the present invention. The Examiner states on pages 4 and 5 of the Office Action that Schoenhard disclose binders with a viscosity above 50,000 mPa, when tested in a 2% aqueous solution; however, the evidence the Examiner points to is a general disclosure of hydroxypropyl methylcellulose (HPMC). Applicants submit that while certain grades of HPMC have viscosities greater than 50,000 mPa, some grades of HPMC are much lower than 50,000 mPa, and therefore the general recitation of HPMC does not render obvious the specific recitation of grades with viscosities above 50,000 mPa. Attached hereto as Exhibit A is an excerpt from the *Handbook of Pharmaceutical Excipients* (3<sup>rd</sup> Ed. 2000) for Hydroxypropyl Methylcellulose showing that the various grades of HPMC exhibit vastly different viscosities (Table II).

Schoenhard discloses the use of delayed release coating agents at pages 17-18 (paragraphs 116-120), including enteric polymers that dissolve in solution at a pH between 5 and 7, and materials that dissolve at higher pH's, such as zein (paragraph 119). However, Schoenhard does not recite any specific combinations of these delayed release agents. Moreover, Schoenhard does not disclose the specific combination of a first pH dependent material that dissolves at a pH between 5 and 7 and a second pH dependent material that dissolves at a pH above 8 (claim 1), above 9 (claims 10 and 35) or at about 11-12 (claim

12). Schoenhard also does not teach a delayed release coating that contains about 20 to about 70 weight percent of an inert processing aid. Additionally, Schoenhard also does not teach the specific ratios of the combined pH dependent materials as recited in Claims 13 and 14 of the present application. Furthermore, Schoenhard does not provide any motivation or suggestion to combine the presently claimed pH dependent materials with a high viscosity hydrogel polymer or with about 20 to about 70 weight percent of an inert processing aid as recited in the pending claims.

Schoenhard also does not disclose the specifically recited percentages of excipients listed in claims 34 and 35 of the present application. Specifically, Schoenhard does not disclose 1-40% of a high viscosity hydrogel binder or 25-90% of a diluent.

The examples disclosed in Schoenhard do not aid a person skilled in the art to arrive at the present invention because all of the examples relevant to tablet formulation relate to compressed controlled release granules, and not to a sustained release tablet with a single core surrounded by a single delayed release coating as claimed in the present application. *See* Example 1 of Schoenhard. Applicants submit that teachings related to coatings on multiparticulate controlled release granules are distinguishable from instructions for coating tablets with a single core and a single delayed release coating because multiparticulate dosage forms have much higher surface areas and therefore different release properties.

The Examiner seeks to correct these major deficiencies in Schoenhard by improperly picking and choosing the missing elements from Mazer, but does not provide any motivation or direction for selecting the specific teachings and combining them with Schoenhard.

Mazer teaches dosage forms that contain multiple beads or pellets wherein the beads

or pellets are coated with at least two different and separate coatings. One of the coatings may be zein and the other coating may comprise enteric polymers. *See* Mazer at Col. 6, lines 6-64.

The Examiner stated on page 5 of the Office Action that Mazer teaches “cores comprising specific percentages of oxycodone and excipients (col. 7).” Applicants submit that there is no teaching in Mazer at col. 7 that recites specific percentages of oxycodone. Moreover, there is no reference to oxycodone anywhere in the Mazer patent.

Further as recited above, while Mazer generally recites the use of HPMC, the general disclosure of HPMC, does not anticipate or render obvious the specific recitation of high viscosity grades of HPMC.

The Examiner has pointed to the disclosure in Mazer and Schoenhard as providing the teaching to combine a first pH dependent material that dissolves at a pH between 5 and 7 with a second pH dependent material that dissolves at a pH above 8. However, the discussion in Mazer cited by the Examiner relating to combining different enteric polymers does not contain a teaching to combine the enteric polymers with zein in a single coating. *See* Mazer at col. 8, lines 15-42. Specifically, Mazer describes two separate coatings wherein the one which may contain zein are “not intended to have enteric characteristics”. *See* Mazer at col. 7, lines 46-50. Therefore Mazer teaches away from combining a first pH dependent material that dissolves at a pH between 5 and 7 with a material such as zein.

The Examiner cites to Mazer for teaching the specific percentage of oxycodone, high viscosity binder and diluent as recited in claims 34-35 of the present application. The Examiner argues that because Mazer teaches dosage forms that contain 80% inactive compounds, a person skilled in the art could arrive at the specific percentage of oxycodone,

high viscosity binder and diluent recited in claims 34-35. *See* Mazer at col. 7, lines 11-17. Applicants submit that this general teaching does not render obvious the excipient ranges recited in claims 34-35. As discussed previously, Mazer does not disclose oxycodone or any weight percentage of oxycodone. Additionally, neither, Schoenhard nor Mazer disclose 1-40% of a high viscosity hydrogel binder in the core of the oxycodone dosage formulation. Finally, neither reference specifically discloses the use of a diluent in the core of the oxycodone formulation at a weight percent of the core of about 25% to about 90%. The general teaching that a dosage form containing excipients which comprise approximately 80% by weight of the dosage form is not a teaching to optimize the excipients until one achieves the specific weight percentages of the presently claimed invention. This is improper hindsight combined with enormous assumptions about optimization.

Further, all of the examples recited in Mazer relate to multiparticulate dosage forms. *See* Examples 1-13 of Mazer. Applicants submit that a combination of Mazer and Schoenhard would result in a multiparticulate dosage form comprising multiple coatings for each individual particle of the dosage form. This would not result in the present invention which recites a single core containing oxycodone and a high viscosity hydrogel polymer surrounded by a single delayed release coating comprising a combination of a first pH dependent material that dissolves at a pH between 5 and 7 and a second pH dependent material that dissolves at a pH above 8, and wherein the delayed release coating contains about 20 to about 70 weight percent of an inert processing aid.

Based upon the foregoing amendments and representations, Applicants respectfully submit that the rejection of the claims in the above-identified application has been overcome and should be withdrawn. Early and favorable action is earnestly solicited.

Respectfully submitted,

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